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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/725,324	11/28/2000	Steven R. Leong	0152.210US	5894

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EXAMINER
SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/725,324	LEONG ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-183* is/are pending in the application.

4a) Of the above claim(s) *1-36,63-83 and 85-183* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,39-62 and 84* is/are rejected.

7)☒ Claim(s) *37-39,47,48,50,51,62 and 84* is/are objected to.

8)☒ Claim(s) *1-183* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,8,11,12*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Sequence Match Listing (2 pages).

DETAILED ACTION

Applicants' election with traverse of Group II (claims 37-62, 84, 123-148, and 170) and sequence election of SEQ ID NO: 8 in Paper No. 19, filed 3/17/03, is acknowledged. Claims 1-36, 63-83, 85-122, 149-169, and 171-183 are withdrawn from consideration as being drawn to non-elected Groups. Claims 123-148 and 170 are withdrawn from consideration as being drawn to non-elected subject matter (sequences).

Applicants' traversal is on the grounds that they should not be subjected to a sequence election requirement of electing only one sequence, that they cannot find this provision that only one sequence is to be examined in the MPEP §803.04 or the USPTO website, that the sequence election requirement is improperly restricting "between" a single claim (citing various case law), and reserve the right to appeal this decision to the Board of Appeals and/or federal courts in the event the restriction requirement is made final.

The applicants' request to withdrawn the sequence election requirement was found unpersuasive because of the following reasons:

The MPEP § 803.04 states the following:

> By statute, "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." **35 U.S.C. 121**. Pursuant to this statute, the rules provide that "[i]f two or more independent and distinct inventions are claimed in a single application, the examiner in his action shall require the applicant . . . to elect that invention to which his claim shall be restricted." **37 CFR 1.142(a)**. See also **37 CFR 1.141(a)**.
>
> Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of **35 U.S.C. 121**. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to **35 U.S.C. 121** and **37 CFR 1.141** *et seq*.

Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of **37 CFR 1.141** *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See *Examination of Patent Applications Containing Nucleotide Sequences,* 1192 O.G. 68 (November 19, 1996).

In the current application, the Examiner has identified more than one patentably distinct invention involving sequences and believes that it is correct to limit the elected claims to one sequence. Applicants are reminded that the current multitude of sequence submissions of examinations at the USPTO has resulted in an undue search burden if more than one sequence is elected.

In their traverse, Applicants cite case law which refers to rejections. No rejections have been set forth as the previous Office action was merely a restriction. Thus, the rejection arguments lack correspondence with the previous written restriction, mailed on 2/14/03.

The requirement is still deemed proper and is therefore made FINAL.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to cytokine polypeptides and nucleic acids, whereas in contrast the elected claims are specifically directed to a cytokine polypeptide.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821 (a)(1) and (a)(2). See for example, claim 45, page 109 (line 27) to page 110 (line 5), and elsewhere. However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825, because SEQ ID Nos cited along with each sequence in the specification. Applicant(s) are required to submit a new computer readable form sequence listing, a paper copy, or CD-ROM for the

specification, statements under 37 CFR § 1.821 (f) and (g), if there is a need to list additional sequences in the sequence listing. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office Action.

Claims herein under examination are 37-62 and 84.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 46, line 31, and elsewhere. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informalities: The second "in" on page 2, line 4, does not make grammatical sense. It appears that "SEQ ID NO: 35", on page 2, line 20, should read "SEQ ID NO: 25." The sentence ending on page 13, line 15, fails to end in a period. There are two consecutive colons on page 13, line 22, which is incorrect punctuation. Correction of these and any other grammatical, spellings, or punctuation mistakes is requested.

Claim Objections

Claims 62 and 84 are objected to because of the following informality: The use of the trademark GENBANK has been noted in these claims. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claims 37-39, 47-48, 50-51, 62, and 84 are objected to due to the inclusion of subject matter which has been non-elected due to restriction requirement and therefore withdrawn from consideration. Claims 40, 49, and 52-61 are also objected to due to their direct or indirect dependence from claims 37 and 48. The non-elected subject matter is summarized as follows: Claim 37 is dependent from non-elected claims directed to nucleic acids. Claims 38-39, 47-48, 50-51, 62, and 84 are directed to including non-elected sequences. Correction is suggested by stating only the subject matter (i.e. SEQ ID NO: 8) which is part of the instant invention.

Claims Rejected Under 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 48-57, 62, and 84 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 48-57, 62, and 84, as written do not sufficiently distinguish over polypeptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hands of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980).

Claim Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 62 and 84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The attempt to incorporate subject matter into this application by reference to GenBank accession numbers in claims 62 and 84 is improper because such material is considered essential

subject matter. Enablement of essential subject matter for the practice of claims cannot be properly supplied by the incorporation by reference of a publication.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

LACK OF WRITTEN DESCRIPTION

Claims 45-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 8 (encoded by SEQ ID NO: 1) which corresponds to a polypeptide sequence. SEQ ID NO: 8 meets the written description provisions of 35 U.S.C. 112, first paragraph. However, claims 45-62 are directed to encompass sequences that have a recited degree of identity, sequences that hybridize to SEQ ID NO: 1, and modified sequences which do not meet the written description provision of 35 U.S.C. 112, first paragraph. Please note the "90% amino acid sequence identity" as recited in claim 45 (line 2), could also

contain sequences including the entire sequence of SEQ ID NO: 8 plus up to 10% of additional sequence on either end of SEQ ID NO: 8 which fails to meet the written description provision of 35 U.S.C. 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by these claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 8, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 8, but not the full breadth of the claims, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-

Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claims Rejected Under 35 U.S.C. § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-40, 46, 48-62, and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 40, 46, 52, 54, 55, 57, 59, 62, and 84 are vague and indefinite due to the unclarity of citing an abbreviation within a word, such as p35, GST, Met, PEGylated, and p40. Correction is suggested by amending in of the full name in parentheses.

Claims 39 and 62 recite the phrase "corresponding to" which is vague and indefinite. It is unclear the corresponding to must be followed. Clarification of the metes and bounds of this claim via clearer claim wording is requested.

Claims 40 and 52 recite the phrase "having T-cell proliferative activity" which is vague and indefinite. It is unclear what criteria and to what extent this criteria must be met to be considered to have such activity. Clarification of the metes and bounds of this claim via clearer claim wording is requested.

Claim 48 recites the phrase "encodes a first polypeptide" which is vague and indefinite. It is unclear what is meant by the terminology of "first polypeptide." Clarification of this phrase

via clearer claim wording is requested. Claims 49-61 are also rejected due to their direct or indirect dependence from claim 48.

Claim 53 recites the phrase "secretion/localization sequence" which is vague and indefinite. It is unclear if the sequence includes the encoding of a secretion *and* localization characteristic or only one of these characteristics, if sequence secretes a substance, if the sequence localizes an entity (and if so, what entity?), or countless other possible scenarios. Clarification of this claim via clearer claim wording is requested. Claim 54 is also rejected due to its dependency from claim 53.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37, 40-46, and 55-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Foss et al (Vet. Immunol. Immunopathol., Vol. 57, 1997, pages 121-134).

Foss et al. disclose a nucleic acid (Figure 1) that encodes a polypeptide which is 90.7% identical to SEQ ID NO: 8 as stated in claim 37 as defined by claims from which it depends. Foss et al. disclose a p40 cytokine polypeptide (Figure 2B, (p)) which contains modifications at equivalent positions of SEQ ID NO: 15 of the instant invention (Figure 2B, (h)). These modifications include substitutions at positions Leu62, Ser71, Gln78, His99, Thr127, Arg130, Glu186, Tyr187, Glu188, Asp196, Met211, Val289, Ser305, Ser307, Arg309, and Gln311 as

well as deletions at residues Arg181 to Asn184 with respect to the equivalent positions to that of SEQ ID NO: 15 as stated in claims 41 and 42. The polypeptide disclosed by Foss et al. comprises one or more substitutions such as Asp40Asn, His91Arg, Thr153Lys, Ser163Thr, Gln166Arg, Ala172Thr, Ala177Glu, Glu178Asp, Arg179Leu, Val180Gly, Asp213Glu, and Gln251His as stated in claim 43. Foss et al. disclose that IL-12 which consists of 35 and 40kDa subunits (abstract) stimulates the proliferation of T cells (page 122, lines 12-13) as stated in claims 40, 44, 46, 58, and 59. Foss et al. disclose the p40 polypeptide (Figure 2B) which is 90.7% identical to SEQ ID NO: 8, a sequence encompassed in the sequence set forth in claim 45. Foss et al. disclose the p40 polypeptide (Figure 2B, (p)) which comprises methionine at the N-terminus as stated in claim 55. Foss et al. disclose IL-12 consists of glycosylated subunits (page 121, lines 1-2) as stated in claims 56 and 57.

Thus, Foss et al. anticipate the limitations in claims 37, 40-46, and 55-59.

Claims 37 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Paoletti et al (P/N 5,833,975).

Paoletti et al. disclose a nucleotide sequence of a p40 expression cassette (SEQ ID NO: 194) which encodes a polypeptide which is 88.5% identical to SEQ ID NO: 8 as stated in claim 37 as defined by claims from which it depends. Paoletti et al. disclose recombinant gene products (abstract). Paoletti disclose cytokine interleukin 12 (IL-12) is a heterodimer composed of 35 kDa and 40 kDa subunits which plays a major role in promoting the T_H1 cell mediated immune response by T-cell proliferative activity (col. 14, lines 4-8 and 47-54) as stated in claim 40. Paoletti disclose recombinant vaccinia virus expressing IL-2 (modified) is attenuated in mice compared to wild-type vaccinia virus due to the ability of the vaccinia-expressed IL-2 to

stimulate mouse NK cells to produce IFNγ (col. 14, lines 11-16). Thus, Paoletti et al. anticipates the limitations in claims 37 and 40.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

May 19, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER